UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,864	11/30/2006	Takashi Shinohara	701067	1275

23460 7590 04/29/2009

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER	
SGAGIAS, MAGDALENE K	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
04/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/594,864	**Applicant(s)** SHINOHARA ET AL.	
	Examiner MAGDALENE K. SGAGIAS	**Art Unit** 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the pre-appeal filed on 3/11/08, PROSECUTION IS HEREBY REOPENED. New art rejections are set forth below.

Applicant's arguments with respect to claims 1-12, 15-16 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1-12, 15-16 are pending and under consideration. Claims 13-14, 17-34 are canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 15-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing multipotent germline stem (mGS) cells, which comprises culturing testis cells using medium containing glial cell derived neurotrophic factor (GDNF), wherein the testis cells contain spermatogonial stem cells (SSCs), and wherein the testis cells are derived from a postnatal mouse, and isolating multipotent gremline stem cells expressing SSEA-1, Forsman antigen , β1-integrin, α6-integrin, EpCAM, CD9, EE2 and c-kit markers, does not reasonably provide enablement for producing pluripotent stem cells derived from postnatal testis of all mammalian species including human species, forming the three somatic lineages. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method of producing pluripotent stem cells, which comprises culturing testis cells using a medium containing glial cell derived neurotrophic factor (GDNF) or an equivalent thereto, wherein the testis cells contain spermatogonial stem cells, and wherein the testis cells are derived from a postnatal mammal, and isolating pluripotent stem cells from the cultured testis cells.

The claims are broad in scope, encompassing a method that would embrace maintaining pluripotency of any mammalian species or human pluripotent cells by culturing testis cells using a medium containing GDNF, LIF, bFGF, feeder cells and the testis cells are p53-deficient. The disclosure provided by the applicant, in view of the prior art, must encompass a wide area of knowledge to a reasonably comprehensive extent. In other word each of those, aspect considered broad must be shown to reasonable extent so that one of the ordinary skills in the art at the time of the invention by applicant would be able to practice the invention without any undue burden being on such artisan.

The specification teaches testis cells were collected from newborn (0-8 days old) ddY mice, DBA/2 mice or transgenic mouse line C57BL6/Tg14 (act-EGFP-Osby01) that was bred into DBA/2 background (designated Green) [0206]. Because these Green mice have the expressed the EGFP gene in substantially all cell types, it is possible to track the cells derived from the mice can be tracked with the fluorescence of EGFP as the indicator [0206]. The specification also teaches for some experiments, testis cells were collected from a newborn p53 deficient mouse in ICR background [0207]. The specification contemplates the pluripotent stem cells obtained by the production method of the present invention have the capability of differentiating into all somatic cells constituting a living organism; all experimental techniques

and methods applicable to ES cells or EG cells can be applied to the pluripotent stem cells; using the pluripotent stem cells, it is possible to produce diverse functional cells, tissues, animals (excluding humans) and the like [0186]. The specification further contemplates that pluripotent stem cells genetically modified it is possible to produce genetically modified diverse functional cells, tissues, animals (excluding humans) and the like [0186]. However, the specification fails to provide guidance for producing pluripotent stem cells as known in the art by forming the three somatic lineages that is by forming endoderm cells, ectoderm cells and mesoderm cells. **Brinster** (Science, 316: 404-405 (IDS)) notes GDNF appears to be a primary regulator of the self-renewal versus differentiation fate decision for mouse and rat SSCs (7, 14), and it is probably a conserved self-renewal signal for all mammalian SSCs and similar to embryonic stem cells (ESCs), SSCs grow in vitro on feeder cells in islands or clumps, and they stain positive for POU domain transcription factor 1 (Oct 3/4) and alkaline phosphatase (p 404, 3rd column). However, Brinster also notes that even these observations suggested that SSCs might be pluripotent, however, whereas ESCs readily generate teratocarcinomas when transplanted in vivo, SSCs do not form tumors under similar conditions and whether the normal adult SSC can be induced to become pluripotent remains controversial. **Turnpenny et al**, (Stem Cells, 24: 212-220, 2006 (IDS)) note the influence of the basic media and feeder layers, all groups reporting hEGC derivation and culture have included other additives and their use originates from mouse pluripotent stem cell derivation and culture however, definitive requirements for any in equivalent hEGC cultures have yet to be established conclusively (p 215, 1st column, under media additives and critical factors). Moreover, Turnpenny et al note there are differences in pluripotent stem cells between mice and humans and despite activation of the LIFR/gp130-STAT3B pathway, LIF (administered in human recombinant form) does not maintain self-renewal of hESCs, which require feeder cells or their conditioned media with an

extracellular matrix (p 215, 2nd column, last paragraph). Turnpenny et al note several groups have noted difficulty in maintaining hEGCs undifferentiated long-term and this problem of undifferentiated status contrasts with other pluripotent stem cell types: hESCs and human embryonal carcinoma cells (hECCs) and mESCs and mEGCs, all of which have been more extensively characterized (p 217, 1st column, 1st paragraph). hEGC cultures have proliferated extensively; however, the proportion of cells expressing pluripotent markers (e.g., OCT4 and stage specific embryonic antigen [SSEA] family members declines over time, variably from 2 to 3 months onwards, and is exacerbated by freeze-thaw routines (p 217, 1st column, 1st paragraph). **Behrouz Aflatoonian et al** (Current Opinion in Biotechnology, 16: 530-535, 2005) note although the pluripotent and proliferative capacity of hEG cells is thought to be equivalent to that of human embryonic stem (hES) cells, there exist difficulties of isolating and maintaining hEG cell lines in vitro (abstract). Aflatoonian notes although the initial generation of hEG cells is relatively simple, the maintenance of well-defined cell lines through extended passage in culture has proved to be quite difficult to date (p 530 2nd column, 1st paragraph). Aflatoonian teaches for instance, just as differences are apparent in the production and maintenance of ES cells from the mouse and human there are also discrepancies in EG cell culture conditions for these species (p 532, 2nd column). Some of the differences appear to relate to inherent cellular adhesive properties of pluripotent cells and their behavior when aggregated or single. For example in the mouse, the inner cell mass or blastocyst can be disaggregated to single cells and ES cell lines derived clonally; similarly, a single-cell suspension obtained from the mouse genital ridge will allow PGC propagation and EG derivation. By contrast, it is well known that hES cells much prefer passage in culture as aggregated plaques if they are to remain undifferentiated (p 532, 2nd column). The complete desegregation of the human genital ridge is more difficult to achieve without compromising PGC survival and EG derivation (p 532,

2nd column). This property of human EG cells also extends to their proliferation where, instead of expanding as a relatively flat colony, hEG cells remain as a compacted mound of cells that is multi-layered and resistant to desegregation procedures and the capacity of human EG cells to be dissociated into small aggregates for passaging, and remain viable and undifferentiated, is therefore very low, hence, the maintenance of hEG cell lines indefinitely and even beyond 15-20 passages is of practical importance if these cell lines are to be uses for cell therapy (p 532, 2nd column bridge to p 533, 1st column).

In light of the above, the state of the art is suggesting that producing pluripotent embryonic stem cells from testis from all mammalian species might be feasible in the future. The instant specification does not provide any relevant teachings, specific guidance, or working examples for overcoming the limitations of maintaining pluripotency of human embryonic stem cells from postnatal testis by forming all three somatic cells lineages in any mammalian species or human raised by the state of the art. Applicants have not provided guidance to overcome the issue of maintaining viable and undifferentiated, pluripotent stem cells is very low, due to incomplete desegregation as raised in the art. Therefore, the skilled artisan would conclude that the state of art of producing pluripotent stem cells from postnatal testis is undeveloped and unpredictable at best. Given the lack of guidance provided by the instant specification, it would have required undue experimentation to practice the invention as claimed for producing pluripotent stem cells from postnatal testis from all mammalian species without a reasonable expectation of success.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above for producing pluripotent stem cells derived from postnatal testis of all mammalian species including human species, forming the three somatic lineages, the lack of direction or guidance provided by the specification for producing pluripotent stem cells derived

from postnatal testis of all mammalian species including human species, forming the three somatic lineages, the absence of working examples for producing pluripotent stem cells derived from postnatal testis of all mammalian species including human species, forming the three somatic lineages, the unpredictable state of the art with respect to producing pluripotent stem cells derived from postnatal testis of all mammalian species including human species, forming the three somatic lineages, the undeveloped state of the art pertaining to producing pluripotent stem cells derived from postnatal testis of all mammalian species including human species, forming the three somatic lineages, and the breadth of the claims directed to all mammalian species, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 rejection under 35 U.S.C. 103(a) as being unpatentable over **Nagano et al,** [Biology of Reproduction, 68: 2207-2214, 2003, (IDS)] in view of **Matsui et al.** [Cell, 70(5): 841-847, 1992, (IDS)] is withdrawn.

Claims **1-2, 4-6, 15** are rejected under 35 U.S.C. 103 (a) as being unpatentable over **Hogan** (US 5,690,926) in views of **Creemers et al,** (Reproduction, 124: 791-799, 2002).

Hogan teaches a method for the isolation of embryonic stem cell lines from postnatal mammalian testis in the presence of feeder cells, leukemia inhibitory factor (LIF)soluble stem

cell factor, and basic fibroblast factor (column 12, lines 61-67 bridge column 13, lines 1-13). Hogan discloses a method of making a mammalian pluripotential embryonic stem cell comprising culturing postnatal mammalian testis in a composition comprising a growth enhancing amount of basic fibroblast growth factor, leukemia inhibitory factor, membrane associated steel factor, and soluble steel factor, thereby making a pluripotential embryonic stem cell from a germ cell (column 6, lines 62-67 bride to column 7, lines 1-3). Hogan discloses "Germ cells" as used herein means the cells which exist in neonatal or postnatal testis and are the progenitors of gametes. In the testis, these germ cells represent a small population of stem cells capable of both self-renewal and differentiation into mature spermatogonia. Thus, "germ cells" are the postnatal equivalent to the prenatal primordial germ cells and can include primitive or immature spermatogonia such as type A spermatogonia or any undifferentiated early stage cell that can form a pluripotent embryonic stem cell (column 7, lines 3-12) (**claim 6** of the instant invention). Hogan also teaches these methods can be practiced utilizing mammal cells including mice, rats, rabbits, guinea pigs, goats, cows, pigs, humans (column 7, lines 13-14). Hogan teaches to determine whether PGCs and their descendants continue to proliferate in culture, primary colonies of PGCs were trypsinized after 6 days in culture and replated on a fresh Sl.sup.4 -m220 <u>feeder layer with added growth factors</u>. By day 6 in secondary culture, large colonies of densely packed alkaline positive (AP) positive cells resembling embryonic stem (ES) cells are present (FIG. 2D, E; FIG. 4, A), and these colonies are also positive for the expression of the <u>antigen SSEA-1</u>, a characteristic of PGCs (column 9, lines 61-67 bridge to column 10) (**claims 2-6, 15** of the instant invention). Hogan differs from the present invention for not teaching glial cell derived neurotrophic factor (GDNF) for producing pluripotent stem cells from postnatal testis.

However, at the time of the instant invention Creemers et al disclose culturing testes cells from testes removed from Nc/CpbU adult or prebubertal mice and isolating type A spermatogonia (p 792, 2nd column, 2nd paragraph). Creemers teaches the type A spermatogonia cells under cultured conditions by adding GDNF to the basic culture media containing bFGF and LIF (p 792 2nd column bridges to p 793, 1st column). Creemers teaches a suspension of type A spermatogonia of which about 10% consists of <u>spermatogonial stem cells,</u> normally comprising only 0.03% of the testicular germ cell population (p 792, 1st column). Creemers teaches comparison of cultures of adult cells with cultures of prepubertal germ cells, commonly used in studies of spermatogenesis, showed that prepubertal germ cells are twice as viable (abstract). Creemers suggests the actual percentage of 58% fro prepubertal mouse germ cells in the present study seems to represent a moderate improvement and additional refinement by adjusting the growth factors concentrations might further enhance viability (p 798, 1st column 2md paragraph). Creemers suggests optimization of the culture of germ cells in defined medium could be achieved by several approaches including the addition to the culture medium the appropriate concentrations of growth factors that might greatly improve viability or proliferation of spermatogonia and the use of well-defined culture conditions for culturing early germ cells is needed for many purposes and merits further studies (p 798, 1st column last paragraph).

Accordingly, in view of the teachings of Creemers it would have been obvious as a design of choice to add GDNF to the culture system of Hogan in order to isolate pluripotent stem cells from postnatal testes in a mouse with a reasonable expectation of success. One of ordinary of skill in the art would have been motivated to do such a modification as Creemers suggests optimization of the culture of germ cells in defined medium could be achieved by the addition of to the culture medium the appropriate concentrations of growth factors that might

greatly improve viability or proliferation of spermatogonia, and the use of well-defined culture conditions for culturing early germ cells is needed for many purposes and merits further studies. One of ordinary of skill in the art would have been particularly motivated to do such a modification as Hogan suggests said cells can be used to derive cells for therapy to treat an abnormal condition. For example, derivatives of human ES cells could be placed in the brain to treat a neurodegenerative disease.

Supreme Court reaffirmed principles based on its precedent that “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” KSR International Co. v. Teleflex Inc. (KSR), 550 U.S. at, 82 USPQ2d at 1395.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Claim **3** is rejected under 35 U.S.C. 103(a) as being unpatentable over **Hogan** (US 5,690,926) in view of **Creemers et al,** (Reproduction, 124: 791-799, 2002) as applied to claims **1-2, 4-6, 15** above, and further in view of **Haneji et al** (J Endorinology, 128(3): 383-8, 1991 taken with **Wahab-Wahlgren** (Mol and Cell Endocrin, 201: 39-46, 2003).

The teachings of Hogan and Creemers apply here as stated above.

Hogan taken with Creemers does not teach EGF in culture media for producing pluripotent stem cells from postnatal testes.

However, at the time of the instant invention Haneji teaches that different concentrations of EGF inhibits the differentiation of type A spermatogonia (p 385, 1st column, figure 2). Wahab-Wahlgren teaches that EGF plays an important role in spermatogonia proliferation in vitro (abstract, and p 44, 1st column, 1st paragraph, discussion).

Accordingly, it would have been obvious for one of ordinary of skill in the art to modify the technology of culturing pluripotent spermatogonial stem cells as taught by the combined references of Hogan/Creemers to include EGF as taught by Haneji taken with Wahab-Wahlgren, with a reasonable expectation of success. One d ordinary of skill in the art would have been motivated to make this modification because Haneji teaches EGF inhibits differentiation of type A spermatogonia. One d ordinary of skill in the art would have been particularly motivated to make this modification in order to maintain the pluripotency of the type spermatogonia stem cells.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Claim **7** is rejected under 35 U.S.C. 103(a) as being unpatentable over **Hogan** (US 5,690,926) in view of **Creemers et al,** (Reproduction, 124: 791-799, 2002) as applied to claims **1-2, 4-6, 15** above, and further in view **Beumer et al** (Cell Death and Differentiation , 5: 669-677, 1998 (IDS)).

Hogan taken with Creemers is applied here as indicated above.

Hogan taken with Creemers, do not teach the testis cells are p53-deficient.

However, at the time the invention was made, Beumer et al teach spermatogonia cell production by the undifferentiated spermatogonia is much more efficient in p53 knock out mice than in wild-type mice, indicating enhanced proliferative activity or less apoptosis of these cells (p 675, 1st column, 1st paragraph). Beumner is an exemplified prior art that teaches that it is routine or well-established in the art to employ p53-deficient testis cells as a source of obtaining SSCs since p53 knock out mice, constitute an increased numbers of spermatogonia (p 670, 1stcolumn, 1st paragraph).

Thus, it would also have been obvious for one of ordinary skill in the art of isolating pluripotent stem cells from mouse testis to further employ p53 knock testis from p53 knock out mice of choice available in the art in order to obtain pluripotnet type A spermatogonial stem cells SSCs from postnatal cultured testis cells of the combined cited references. One of ordinary skill in the art would have been motivated to employ p53 deficient testis cells in the system of Hogan/Creemers in order to increase the number of undifferentiated SSCs as taught by Beumer. One of ordinary skill in the art would have reasonably expected that inclusion of p53 deficient testis cells are routinely employed in the art and can help to further isolate pluripotent stem cells from mouse testis particularly in view of the totality of the prior art at the time the invention was made.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Claim **16** is rejected under 35 U.S.C. 103(a) as being unpatentable over **Hogan** (US 5,690,926) taken with **Creemers et al,** (Reproduction, 124: 791-799, 2002) and further in view of **Kanatsu-Shinohara et al, [**Biology of Reproduction 70, 70–75 ,2004, (IDS)]; **Shinohara et al,** [PNAS, 96: 5504-5509, 1999, (IDS)]; **Van Der Wee et al** (Journal of Andrology, 22(4): 696-704, 2001).

The teachings of Hogan/Creemers is applied here as indicated above.

Hogan/Creemers does not teach the pluripotent stem cells are positive for CD9, β1- and α6-integrin, Ep-CAM and c-kit surface markers.

However, at the time of the instant invention Kanatsu-Shinohara et al, teach spermatogonial stem cells can be enriched by selection with an antibody against cell-surface molecules. Kanatsu-Shinohara teaches spermatogonial stem cells express the surface CD9 molecule, which is commonly expressed on stem cells of other tissues (abstract). Selection of

both mouse and rat testis cells with anti-CD9 antibody resulted in 5- to 7-fold enrichment of spermatogonial stem cells from intact testis cells, indicating that CD9 is commonly expressed on spermatogonial stem cells of both species (abstract). Therefore, CD9 may be involved in the common machinery in stem cells of many self-renewing tissues, and the identification of a common surface antigen on spermatogonial stem cells of different species has important implications for the development of a technique to enrich stem cells from other mammalian species (abstract). As such Kanatsu-Shinohara et al, provide sufficient motivation to enrich pluripotent stem cells by the use of the CD9 marker as taught by Kanatsu-Shinohara et al. Shinohara et al, supplements the teachings of Kanatsu-Shinohara et al, by teaching SSCs also express the surface markers β1- and a6 integrin (title). Shinohara suggests the degree of enrichment of stem cells attainable by this method will allow further fractionation and analysis of the enriched cell population to identify a set of additional antigens characteristic of and unique for spermatogonial stem cells (p 5509, 1st column, 1st paragraph). A systematic evaluation of surface molecules on the stem cell will facilitate identification and purification of these cells and greatly contribute to our understanding of their biology and survival requirements. This approach mirrors developments made with hematopoietic stem cells during the last decade. As stem cell markers are identified, enrichment for stem cell populations can be increased, facilitating their eventual purification. **Van Der Wee** teaches the isolation of type A spermatogonia using magnetic beads and antibodies that recognize the c-kit receptor or the Ep-CAM (abstract).

Accordingly, in view of the teachings of Kanatsu-Shinohara/Shinohara/ **Van Der Wee**, it would have been obvious for one of ordinary of skill in the art to use the SSC surface markers of CD9, β1- and a6 integrin, c-kit and Ep-CAM for the production of enriched pluripotent stem cells from testis cells by modifying the system of the combined references in the art. One of ordinary of skill in the art would have been sufficiently motivated for such a modification since it was art

goal to produce enriched pluripotent stem cells from testicular SSCs via cell surface markers using fluorescence sorting from all different species particularly in view of the totality of the prior art at the time the invention was made. Kanatsu-Shinohara/Shinohara/ **Van Der Wee** provide teachings, suggestion, and motivation to perform the instantly claimed methods.

Even though, the combined references do not teach the Forsman antigen and EE2 marker the cultured pluripotent cells of the combined cited references would inherently carry said surface markers.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Applicant's arguments are moot in view of new grounds of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 12 of copending Application No. 10/553,118 is withdrawn.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Magdalene K. Sgagias
Art Unit 1632

/Anne-Marie Falk/
Anne-Marie Falk, Ph.D.
Primary Examiner, Art Unit 1632

/Peter Paras, Jr./
Supervisory Patent Examiner, Art Unit 1632